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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,032	06/20/2003	David J. Hammond	70065.0003USU1	5177

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EXAMINER	
STEELE, AMBER D	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
12/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/601,032	HAMMOND ET AL.	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,19,21-24 and 28* is/are pending in the application.

4a) Of the above claim(s) *7-10,13,16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,11,12,14,15,19,21-24 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The amendment to the claims received on February 5, 2007 amended claims 1 and 12 and canceled claim 18.

The amendment to the claims received on September 25, 2007 amended claim 1, canceled claims 20 and 25-27, and added new claim 28.

Claims 1-17, 19, 21-24, and 28 are currently pending.

Claims 1-6, 11-12, 14-15, 19, 21-24, and 28 are currently under consideration.

Election/Restrictions

2. The elections by applicants in the response received on May 10, 2006 are reiterated: election with traverse of Group I (present claims 1-17, 19, 21-24, and 28) and election without traverse of conditioned cell medium as the species of mixture/composition and cell proliferation as the species of activity.

The requirement was deemed proper and made FINAL in the Office action mailed on August 3, 2006.

3. Claims 7-10, 13, and 16-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on May 10, 2006.

Priority

4. The present application claims benefit of U.S. provisional application 60/395,038 filed on July 11, 2002.

Invention as Claimed

5. A method of screening a mixture for active entities, which method comprises: (i) providing a plurality of different ligands, wherein each ligand is attached to a support to form a plurality of ligand-support complexes, (ii) contacting the ligand-support complexes with a mixture comprising a plurality of entities under conditions that allow at least one entity to bind to at least one ligand-support complex, thereby forming more than one entity-ligand-support complex, (iii) separating more than one entity-ligand-support complex from the unbound entities, (iv) assaying an activity of the entity, wherein the entity may be dissociated partially or completely from the entity-ligand-support complex separated in step (iii) and wherein the activity assayed is not solely binding of the entity to the ligand-support complex, (v) detecting the activity, (vi) selecting at least one entity-ligand-support-complex that bound the entity that exhibited the detected activity, and (vii) determining the chemical identity of at least one ligand to which said entity that exhibits the detected activity binds whereupon a mixture is screened for active entities and variations thereof.

Withdrawn Objection

6. The objection to the disclosure regarding the lack of a SEQ ID NO: for the hexapeptide HPQFLS (see the second to last line of paragraph 62) is withdrawn in view of the amendment to the specification received on September 25, 2007.

Withdrawn Rejections

7. The rejection of claims 1-6, 11-12, 14-15, and 19-24 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn upon further consideration.

8. The rejection of claims 1-5 and 11-12 under 35 U.S.C. 102(b) as being anticipated by Baumbach et al. BioPharm. May 1992 pages 24-31 (submitted in IDS) is withdrawn in view of the amendment to the claims incorporating the limitation of previous claim 20 into independent claim 1.

Maintained Rejection

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. In addition, the text of the claims may have been altered to reflect the claim amendments received on September 25, 2007.

Claim Rejections - 35 USC § 103

10. Claims 1-6, 11-12, 14-15, 19, 21-24, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al. Analytical Biochemistry 294: 55-62, July 1, 2001 and Lam et al. U.S. Patent 5,510,240 issued April 23, 1996.

For present claims 1-2, 4-6, and 11-12, Huang et al. teach methods for simultaneous detection of multiple cytokines from conditioned media and patient's sera by an antibody-based protein array system comprising (i) adding capture antibodies (i.e. ligands; proteins) onto a Hybond ECL membrane (i.e. support; nitrocellulose) wherein different antibodies (i.e. plurality of different ligands) can be utilized and the membrane can be cut into strips thus creating a plurality of ligand-support complexes, (ii) contacting the ligand-support complexes with conditioned medium or patient sera (i.e. mixture comprising a plurality of entities; protein, antibody, cell, organic compound, protein complex, bacteria, virus, etc. entities) thus creating an entity-ligand-support complex or more than one entity-ligand-support complexes wherein more than one membrane strip is utilized, (iii) washing to remove non-bound entities (i.e. separating),

(iv) assaying for binding (i.e. physical activity), (v) detecting binding, and selecting the "binders" (please refer to the entire references particularly the "Methods" section).

However, Huang et al. does not specifically teach detecting an activity other than binding.

For present claims 1 and 28, Lam et al. teach methods of screening peptide libraries utilizing a library of bio-oligomers (i.e. entities) attached to solid phase supports, introducing an acceptor molecules or substrate molecule including antibodies which can be bound onto solid phase support (i.e. ligand-support; column 18, lines 30-36) that recognizes and binds the bio-oligomer (i.e. entity), washing nonbound molecules from the mixture, assaying for binding and biological/physical/chemical/biochemical reactions including enzyme activity, toxicity, growth promotion, etc., detecting binding and the biological/physical/chemical/biochemical reactions, and isolating a support/bio-oligomer/molecule with the desired property including binding, stimulation, inhibition, toxicity, growth, proliferation, etc. (e.g. activity) (please refer to abstract; sections 1, 3, 5.1, 5.4, 5.5 including 5.5.1-5.5.3; Example sections 6-14; Figures 1-2 and 4-8D). In addition, Lam et al. teach identifying peptide sequences including sequencing (please refer to section 5.5.2; Tables 1-5; Examples 10-13). Furthermore, Lam et al. teach that each support can have multiple copies of different ligands wherein each bead has a different ligand or bio-oligomer (i.e. one bead one bio-oligomer; please refer to Figure 1; sections 1; columns 5-8 and 10-11).

For present claims 2-3, Lam et al. teach that the ligands can be peptides or nucleic acids (please refer to sections 5.1, 5.2, 5.3).

For present claim 4, Lam et al. teach that the supports can be silica, resin, plastic films, glass beads, alumina gels, polystyrene, polydimethylacrylamide (e.g. polymethacrylate; please refer to section 5.4).

For present claims 5-6, Lam et al. teach that the cells and conditioned culture medium can be utilized in the screening methods (please refer to sections 5.5.2.1).

For present claim 11, Lam et al. teach that the molecule (e.g. entity) can be protein, antibody, enzyme, cell, receptor, virus, carbohydrate, drugs, lipids (please refer to sections 5.5, 5.5.1).

For present claims 12 and 14-15, Lam et al. teach determining activities including binding, stimulation, inhibition, toxicity, enzyme activity, killing, growth promotion, proliferation, or physiological change (please refer to sections 5.5 including 5.5.1, 5.5.2).

For present claim 19, Lam et al. teach that the beads can be partitioned and separated into smaller pools (e.g. subpools; please refer to sections 5.5.1, 5.5.2).

For present claims 21 and 22, Lam et al. teach that the screening assay can repeated several times and that cleavable linkers can be utilized to recover the peptides bound to the supports (sections 5.1, 5.5.1, 5.5.2, 5.4).

For present claim 23, Lam et al. teach identifying peptide sequences including sequencing (please refer to section 5.5.2; Tables 1-5; Examples 10-13).

For present claim 24, Lam et al. teach that cleavage and/or release of the components of the molecule-peptide-support is possible (please refer to 5.1, 5.5.1, 5.5.2, 5.4).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the methods for simultaneous detection of multiple cytokines

from conditioned media and patient's sera by an antibody-based protein array system taught by Huang et al. with the methods taught by Lam et al. combining methods for screening for binding and other "activities".

One having ordinary skill in the art would have been motivated to do this because it would be a natural progression in the experimental process as exemplified by Lam et al. (see below) to find an entity and then determine what the activity of the entity is (i.e. screen for a molecule via binding then screen for other activities). Huang et al. teach that the cytokines they screened for binding play important roles in innate immunity, apoptosis, angiogenesis, cell growth, and cell differentiation (i.e. activities known or previously screened for; please refer to page 61, left column, last paragraph). In addition, Lam et al. teach methods of screening peptide libraries utilizing a library of bio-oligomers (i.e. entities) attached to solid phase supports for binding and biological, physical, chemical, and/or biochemical reactions including enzyme activity, toxicity, growth promotion, etc. (i.e. activity; please refer to abstract; sections 1, 3, 5.1, 5.4, 5.5 including 5.5.1-5.5.3; Example sections 6-14; Figures 1-2 and 4-8D; all of which disclose the natural progression for finding an entity and then determining what the activity of that entity is).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the methods for simultaneous detection of multiple cytokines from conditioned media and patient's sera by an antibody-based protein array system taught by Huang et al. with the methods taught by Lam et al. combining methods for screening for binding and other "activities" because Huang et al. teach that the cytokines they screened for binding play

important roles in innate immunity, apoptosis, angiogenesis, cell growth, and cell differentiation (please refer to page 61, left column, last paragraph).

Therefore, the modification of the methods for simultaneous detection of multiple cytokines from conditioned media and patient's sera by an antibody-based protein array system taught by Huang et al. with the methods taught by Lam et al. combining methods for screening for binding and other "activities" render the instant claims *prima facie* obvious.

Arguments and Response

11. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Huang et al. Analytical Biochemistry 294: 55-62, July 1, 2001 and Lam et al. U.S. Patent 5,510,240 issued April 23, 1996 for claims 1-6, 11-12, 14-15, 19, 21-24, and 28 were considered but are not persuasive for the following reasons.

Applicants contend that the ligands of Huang et al. are already known, Lam et al. assays the activity of the ligand and not the acceptor molecule (i.e. does not teach assaying the activity of the entity), Lam et al. does not teach "assaying the activity of the entity wherein the entity may be dissociated partially or completely from an entity-ligand-support complex separated in step (iii)", Lam et al. does not teach "selecting...the entity-ligand-support complex that bound the entity that exhibited the detected activity", and the modification of Huang et al. in view of Lam et al. would be inoperative because Huang et al. knows the identity of the antibodies and Lam et al. knows the identity of the entity which is used to identify the bio-oligomer ligand (i.e. argument based on whether the entity or the bio-oligomer is on the solid support, whether the "known" entity is on the solid support or the "unknown" entity is on the solid support). In addition, applicants contend that the examiner has not provided a motivation statement.

Applicants' arguments are not convincing since the teachings of Huang et al. and Lam et al. render the method of the instant claims *prima facie* obvious.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. identity of ligand is unknown until method step vii) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Lam et al. teach "assaying the activity of the entity wherein the entity may be dissociated partially or completely from an entity-ligand-support complex separated in step (iii)" via cleavage of the bio-oligomer from the support, releasing the bio-oligomer from the combination in situ and assaying for biological activity in situ after binding, physically isolating the bio-oligomer of interest (please refer to the entire specification particularly column 5, lines 19-42; sections 5.4, 5.5.1, 5.5.2).

Lam et al. teach "selecting...the entity-ligand-support complex that bound the entity that exhibited the detected activity" via subpooling, identifying and isolating acceptor/bio-oligomer/support complexes, and physically isolating the complexes of interest (please refer to the entire specification particularly sections 5.5, 5.5.1).

It would be obvious to one of skill in the art to provide either the known or unknown entity on the solid support. Lam et al. teach utilizing random bio-oligomer libraries to identify a ligand (i.e. bio-oligomer) that binds an acceptor molecule wherein the bio-oligomer can be a peptide, an oligonucleotide, etc. and the acceptor can be a peptide, an oligonucleotide, antibodies, receptors, viruses, proteins, carbohydrates, nucleic acids, lipids, drugs, metals, small molecules, or any biological macromolecule (i.e. acceptor and ligand reversible; please refer to column 4, lines 51-57; column 5, lines 1-18; sections 5, 5.1, 5.2, 5.3, 5.5.1). Furthermore, Lam et al. teach a biooligomer bound to a support which is then screened with an antibody bound to a support wherein the antibody binds to the bio-oligomer then the biooligomer can be cleaved from the support and assayed for an activity (please refer to section 5.5 particularly column 18, section ii).

The motivation is as follows: One having ordinary skill in the art would have been motivated to do this because it would be a natural progression in the experimental process as exemplified by Lam et al. (see below) to find an entity and then determine what the activity of the entity is (i.e. screen for a molecule via binding then screen for other activities). Huang et al. teach that the cytokines they screened for binding play important roles in innate immunity, apoptosis, angiogenesis, cell growth, and cell differentiation (i.e. activities known or previously screened for; please refer to page 61, left column, last paragraph). In addition, Lam et al. teach methods of screening peptide libraries utilizing a library of bio-oligomers (i.e. entities) attached to solid phase supports for binding and biological, physical, chemical, and/or biochemical reactions including enzyme activity, toxicity, growth promotion, etc. (i.e. activity; please refer to abstract; sections 1, 3, 5.1, 5.4, 5.5 including 5.5.1-5.5.3; Example sections 6-14; Figures 1-2 and

4-8D; all of which disclose the natural progression for finding an entity and then determining what the activity of that entity is).

Conclusion

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ADS
November 26, 2007

/Jon D. Epperson/
Primary Examiner, AU 1639